

REMARKS/ARGUMENTS

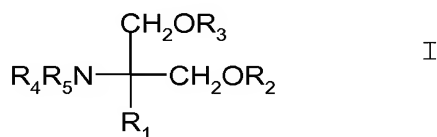
Claims 12 to 16 are presently pending in this patent application. Claims 1 to 11 have been cancelled, without prejudice. Applicants reserve the right to pursue subject matter that remains after the prosecution of the present application in a future continuing patent application, for example, a division.

Discussion of the Rejections under 35 U.S.C. § 103(a)

Claims 12 to 16 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 6,187,821 to Fujita et al. ("Fujita") in view of www.mult-sclerosis.org/opticneuritis.html ("the ON website") and U.S. Patent No. 5,138,051 to Hughes ("Hughes"). Applicants respectfully traverse the rejection as the ON website is not available as a prior art reference and, the combination of Fujita, Hughes and the ON website (*arguendo*) does not produce the presently claimed invention.

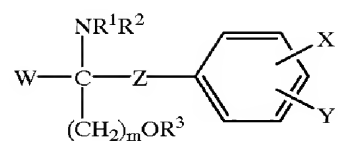
"A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field" (*In re Kotzab*, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000)). "The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time" (*In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999) (quoting *Interconnect Planning Corp. v. Feil*, 227 U.S.P.Q. 543, 547 (Fed. Cir. 1985)). To establish a *prima facie* case of obviousness, the examiner must show reasons that the skilled artisan, with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed (see *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1458 (Fed. Cir. 1998)).

Applicants' claims define, in part, a "method for treating, alleviating or delaying the progression of optic neuritis in a subject in need thereof comprising administering an S1P receptor agonist of formula (I)



..." (see e.g. claim 12). Applicants' claims further define methods for "treating, alleviating or delaying the progression of optic neuritis" comprising administering a compound of formula (I) in combination with "at least one co-agent shown to have clinical activity against at least one symptom of a demyelinating disease", such as an mTOR inhibitor (see e.g. claims 14, 15).

In contrast, Fujita discloses methods for the prevention and treatment of at least 180 different diseases, including multiple sclerosis, comprising administering compounds of formula I



(see Fujita at Col. 2, lines 25 to 67, Col. 3, lines 1 to 5, Col. 79, lines 61 to 67, Col. 80, lines 1 to 67, Col. 81, lines 1 to 55). Fujita does not disclose or suggest the treatment of optic neuritis.

The Action adds Hughes to Fujita for the teaching that rapamycin, an mTOR inhibitor, is effective in an experimental model for multiple sclerosis (Action at 5). Hughes thus discloses preliminary evidence that rapamycin may be useful for the treatment of multiple sclerosis. Hughes, like Fujita, does not disclose the treatment of optic neuritis, or the use of applicants' disclosed compounds to treat optic neuritis alone or in combination with any co-agent. The Action does not provide any evidence to show why one of ordinary skill in the art, when presented with the disclosures of Fujita and Hughes at the time of the present invention, would be motivated to use an S1P receptor agonist, alone or in combination with a co-agent, to treat optic neuritis, as defined by applicants' claimed invention. Claims 12 to 16 are thus patentable over the combination of Fujita and Hughes.

The Action also combines Fujita and Hughes with the ON website. In the first instance, the ON website is not available as prior art under 35 U.S.C. § 103(a) as it was published after the effective filing date of the presently claimed invention. A reference is available as prior art under § 103 when it qualifies as prior art under § 102 (see MPEP § 2141.01). Under § 102, a non-patent reference must be published before the effective filing date of an application to qualify as prior art (see MPEP § 706.02). In particular, the present application was filed on May 17, 2005 as a U.S. national stage application of PCT Application No. PCT/EP03/10579, filed on September 23, 2003 ("the '579 application"). The presently claimed invention is fully supported by the '579 application in, for example, the claims and the specification at pages 2-5 and 12-18. Accordingly, the effective filing date of the presently claimed invention is September 23, 2003. The content of the ON website, however, was published on January 21, 2008. The presently claimed invention thus antedates the ON website. As such, the ON website does not qualify as a § 102/§ 103 reference. Accordingly, reconsideration and withdrawal of the rejection are requested respectfully for at least this reason.

Although Applicants do not concede that the ON website is available as a prior art reference, or that Fujita and Hughes can be combined with the ON website, the combination of Fujita, Hughes and the ON website (*arguendo*) does not produce the presently claimed invention. The ON website asserts that "optic neuritis is an inflammation with accompanying demyelination of the optic nerve, and is one of the most frequently presenting symptoms of multiple sclerosis" (Action at 5). The ON website therefore discloses that although optic neuritis may be associated with multiple sclerosis, optic neuritis is not necessarily present in conjunction with multiple sclerosis. Further, optic neuritis is recognized in the art as a separate disease.

Fujita and Hughes' disclosure of multiple sclerosis treatment is thus not a teaching of optic neuritis treatment. The combination of Fujita and Hughes with the ON website still does not provide any evidence to show why one of ordinary skill in the art, when presented with the disclosures of Fujita, Hughes and the ON website at the time of the present invention (*arguendo*), would be motivated to use applicants' S1P receptor agonists to treat optic neuritis, as defined by applicants' claimed invention.

Indeed, the Patent Office has the burden of presenting factual evidence that would indicate that the claimed methods are prima facie obvious (*In re Lunsford*, 148 U.S.P.Q. 721 (C.C.P.A. 1966)). In the absence of such a showing, such a rejection is based upon impermissible hindsight (*In re Fritch*, 23 U.S.P.Q.2d 1780, 1784 (Fed. Cir. 1992) ("it is impermissible for an Examiner, in proffering a 35 U.S.C. § 103 rejection, to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art to render the claimed invention obvious.")). Accordingly, reconsideration and withdrawal of the rejection are requested respectfully for at least this reason.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Action of record. If there are any issues that can be resolved by a telephone conference, the Examiner is invited to telephone the undersigned attorney.

It is hereby requested that the term to respond to the Action of June 25, 2008 be extended pursuant to 37 C.F.R. § 1.136(a) for three (3) months, from September 25, 2008 to December 29, 2008 (December 25, 2008 and December 26, 2008 are Federal Holidays and December 27, 2008 is a Saturday). The Commissioner is hereby authorized to charge any fees required to Deposit Account No. **19-0134** in the name of Novartis.

Respectfully submitted,

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Date: December 29, 2008

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